2020-05-29

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10.1111/jebm.12391
Journal of Evidence-Based Medicine
Wiley

DOI: 10.1111/jebm.12391

WILEY

PERSPECTIVE

Designing clinical trials for future space missions as a pathway to changing how clinical trials are conducted on Earth

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Abstract

Objective: The project aims to build a framework for conducting clinical trials for long-term interplanetary missions to contribute to innovation in clinical trials on Earth, especially around patient involvement and ownership.

Methods: We conducted two workshops in which participants were immersed in the speculative scenario of an interplanetary mission in which health problems emerged that required medical trials to resolve. The workshops used virtual reality and live simulation to mimic a zero-gravity environment and visual perception shifts and were followed by group discussion.

Results: Some key aspects for the framework that emerged from the workshops included: (a) approaches to be inclusive in the management of the trial, (b) approaches to be inclusive in designing the research project (patient preference trials, n-of-1 trials, designing clinical trials to be part of a future prospective meta-analysis, etc), (c) balancing the research needs and the community needs (eg, allocation of the participants based on both research and community need), (d) ethics and partnerships (ethics and consent issues and how they relate to partnerships and relationships).

Conclusion: In identifying some key areas that need to be incorporated in future planning of clinical trials for interplanetary missions, we also identified areas that are relevant to engaging patients in clinical trials on Earth. We will suggest using the same methodology to facilitate more in-depth discussions on specific aspects of clinical trials in aerospace medicine. The methodology can be more widely used in other areas to open new inclusive conversations around innovating research methodology.

KEYWORDS

clinical trial methodology, clinical trial, evidence-based healthcare, medical simulation, research methodology, space mission

1 | INTRODUCTION

On Earth, randomized controlled trials (RCT) are considered to provide the best available evidence to inform decisions on the effectiveness of medical treatments. These trials are usually repeated across the world on different populations with numbers of participants ranging in size and might be up to several thousand. This provides robust data indicating whether effectiveness can be generalized. In aerospace

medicine, the number of astronauts is limited so commissioning large clinical trials is challenging, resulting in either small case studies or simulating space conditions on Earth to provide additional numbers and facilitate randomization. Additionally, due to the environment and lack of gravity, there will be new questions when randomization to the control group is detrimental to health and consequently unethical.

Future research for space exploration will not only require repeating terrestrial research in simulated/space environments, it also requires innovative approaches to the methods of clinical research to investigate these new challenges. Long-term missions require the continuous commitment and motivation of participants in the clinical trial; therefore patient involvement in the research process is more important. In this project, we developed and piloted a new approach—speculative theorization using simulation (including virtual reality [VR] and live-simulation) grounded in evidence synthesis. The project used speculative theorization to identify new methods to study complex applied clinical research questions and engage with a more diverse group of individuals from different disciplines and experiences. This pilot focused on a specific research topic—conducting clinical trials for the health of astronauts in micro, or partial, gravity. As the project developed, we realized the speculative theorization is also a beneficial thought experiment to encourage trialists, practitioners and members of the public to think more seriously about how to design inclusive clinical trials in partnerships about patients due to the restrictive nature of the scenario—you have to design the trial in a way that all or at least more participants agree to participate and also consider the social and cultural implications of the trial on the community.

The project started a few systematic reviews[1-3] around specific questions in aerospace medicine that highlighted some issues around systematic reviews and primary studies in aerospace medicine. The methods to synthesize evidence on a focused health research question are well documented in the literature.[4,5] However, there are specific challenges in reviews of aerospace medicine that we observed in previous reviews,[1,2] like databases and resources to search for studies (Table 1). The other issues are highlighted in Table 2. Systematic reviews will use certain structure likes PICO (stands for participants/population, intervention, comparison, outcome) to focus the research question. In the case of systematic reviews in aerospace medicine, the population are usually either astronauts, space tourists or individuals participating in simulated studies attempting to replicate a certain aspect of space missions. In the previous reviews that we were involved, the outcome measurements that were predominately used in the included studies (and to our knowledge in a lot of space operations) are biomedical or physiological outcomes. We raised the need to include patient-relevant outcomes in these trials, and it was also a topic that came up in this project.

These issues might be a reflection of the culture of medicine in space is predominantly top-down, that is, astronauts are required to do all manner of medical tests and have them performed on themselves in order to be astronauts. The Mars scenario fundamentally challenges the space industry culture of medical tests. However, this proposed culture-shift to an all-inclusive test paradigm for crews also begs questions of the culture of medical trials as they are on Earth and the capacity to change the existing structures and frameworks. At this stage, it is also worth mentioning a current recent incidence related to the communication between an astronaut and his clinician. Chris Hadfield talks in his book about how a panel of surgeons decided on surgery for him without consulting him before his last mission to International Space Station. He resisted the decision as there was inadequate evidence to support it. This example demonstrates the different values and preferences of the person involved and the managers in situations when the evidence is uncertain.[6]

This study uses a methodological approach that shares traits with speculative and critical design, using imagined scenarios, props, imagery, and diegetic prototypes to raise questions regarding preferable futures. These design methods often take inspiration from science/speculative fiction as a way to trigger debate and discussion.[7] The influence of art and culture (including futuristic media) may shape or influence our vision of the future and even guide the design of medical products, but currently there are few visions of future medical research that encompasses innovation of methods of clinical research.

To build the scenario for this workshop that is both future-facing as well as retaining and drawing from present medical knowledge, the experience and questions contained tropes from both science fiction as well as tropes from the history of clinical trials. An example that influenced the scenario built for this workshop is that of sailors affected by scurvy on naval vessels in the 17th century, a situation that shares resemblances to the conundrum of clinical trials in space missions.[8] Popular science fiction movies can shape or influence our imagination for the future but do not engage all aspects of medical research development. For example, the Qualcomm Tricorder X-prize has been awarded to a family-led team to develop a medical device that intended to develop technologies to diagnose a set of 13 medical conditions independent of health professionals or facilities and continuously measure five vital signs in 2017. The idea was inspired by the popular science fiction series Star Trek. In the Star Trek series and similar sci-fi movies and series, a doctor uses complex technologies to make very accurate diagnoses (through micro- and nanotechnologies, data and information) and often finds a treatment to cure the problem/disease (in lots of cases to total health without adverse events). In this and similar popular sci-fi movies and series, the storyline emphasizes the increasing accuracy of diagnostic technologies and the skill and genius of the doctor. Less attention is given to the possibilities of using innovative clinical trial research methods in space missions. The conundrum of clinical trials in space missions and the scenario explored in this workshop has a lot of similarities to the historical scenario of sailors affected by scurvy on navy ships in the 17th century. The standard method of proposing medical treatments (skillful and smart doctors, suggesting treatments based on experience) generated several possible treatments for scurvy. However, there were still uncertainties as to which treatments work best to treat scurvy. The mortality and morbidity of scurvy between sailors were still high. James Lind was a navy doctor who trawled the literature and anecdotal advice on treatments and then conducted a small controlled clinical trial to identify an effective treatment. The latter provided evidence to combat the existing conflict and uncertainty.[8]

TABLE 1 Space research specific databases

Electronic database	Description
Space Life Sciences NLM subset	https://www.nlm.nih.gov/databases/databases_space.html This is a subset of the US National Library of Medicine.
NASA Scientific and Technical Information (STI) Program	https://www.sti.nasa.gov/ This is a database of citations, documents and images created or funded by NASA or its predecessor NACA. It is searchable via the Technical Reports Server (NTRS): https://ntrs.nasa.gov/advSearch.jsp
PubSpace	https://www.nasa.gov/open/researchaccess/pubspace This is an archive of NASA-funded research publications which are made available to the public via the PubMed Central platform.
ESA—Erasmus Experiment Archive (EEA)	http://eea.spaceflight.esa.int/portal/ This is an archive of ESA-funded research experiments, independent of any subsequent publication as journal articles.
NASA—Life Science Data Archive (LSDA)	https://lsda.jsc.nasa.gov/ This is an archive of the biomedical experiments conducted by NASA including the Human Research Program.
DLR—German Aerospace Centre	http://elib.dlr.de/cgi/search/advanced This is an online collection of conference abstracts, reports and citations of some published journal articles. There is no explicit collection policy.
Canadian Space Agency	Canadian space agency does not seem to have a database associated with their work. They have a publication section that includes audits and reports and they have an open access data portal http://www.asc-csa.gc.ca/eng/open-data/access-the-data.asp#life-sciences. The open data portal at the moment has only one type of life sciences data – performance readiness evaluation and training tool.
International Space University	The library of the university has its own database and provides advanced search option available. However, it is unclear what the process of selecting, archiving and indexing of the resources in the database https://isulibrary.isunet.edu/
British Antarctic Survey	We will expect that some reviews might include Antarctic missions as a simulated environment. The British Antarctic Survey has a meta-data section including human factors although currently has zero entries https://data.bas.ac.uk/
Other online sources	
Austrian Space Forums (Österreichisches Weltraum Forum)	They conduct planetary analog mission research and if that type of simulation studies are included in the review, it is helpful to check the website https://oewf.org/
British Interplanetary Society (BIS)	The Society produces two journals that can include research publications that will not be picked up in other databases that we search in systematic reviews https://www.bis-space.com/what-we-do/publications
NASA evidence book	NASA human research program is a collection of evidence based risk reports. Unfortunately, there is not enough detail on the methods of these evidence books available to judge their quality. However, they can be a resource to identify research based on what they have cited or use in the documentation https://humanresearchroadmap.nasa.gov/evidence/
The Japanese Aerospace Exploration Agency (JAXA)	The agency does not seem to be have a database for identification of articles but has a list of experiments that they are involved in—this includes ones around medical experimentation. http://iss.jaxa.jp/en/kiboexp/
A list of conferences and meetings with relevant research abstracts	
■ Aerospace medicine associated (ASMS) Annual Conference ■ International Astronautical Congress ■ European Low Gravity Research Association Conference ■ World Extreme Medicine Conference ■ UK Space Environments Conference ■ Astrobiology Society of Britain Conference ■ The International Congress of Aviation and Space Medicine (ICASM) ■ International Conference on Astrobiology (AstroBioCon) ■ Annual International Space Station R&D Conference	

There is a need to reconceptualize clinical trials in interplanetary space missions because of how potentially different conditions would be between living on Earth and settling on other planets, for example, Mars. These include physical aspects such as partial gravity or a different atmosphere, along with the psychological and social issues of small and isolated populations. This small and isolated community can be simulated with smaller numbers of humans; however, there are other challenges about the relationship between individuals, patients, clinicians, and trials that introduce new problems. Moreover, risks associated with the decisions and their consequences have

TABLE 2 Methodological gaps from previous systematic reviews

Systematic review	Methodological gaps
Winnard A 2017[1]	Lack of consistency in reporting outcomes measures and the focus on biomedical measurements instead of patient relevant ones All studies were indirect simulation studies with heterogeneous context and delivery of intervention that introduced challenged both in synthesizing the evidence or judging its applicability and generalizability Currently, high-quality studies done on astronaut are not available. Due to small number of astronauts in each mission, the studies are usually not in the form of clinical trials
Richter C 2017[2]	It has similar gaps to the previous one. In addition to this, the issue of finding the threshold for gravity that has the least problematic impact on the human body which requires regression analysis and exposure of different types of gravities. In relation to this project, we can translate the issue of changes in gravity on the human body to get to Mars; from earth gravity to microgravity and then the partial gravity on Mars.

different implications in space that can affect the decision-making process.

2 | METHODS

We designed a creative workshop that included a simulation of a disaster during a space mission, the usage of optical design to distort vision and an interactive methodological discussion. The workshop was based on the topics identified from previous systematic reviews (Table 2) and the speculative theorization around clinical trials in space missions. It intended to create altered states such as a different weight and different perspective to jolt participants into imagining the realities of astronauts.

The workshop was shaped around a speculative scenario (Table 3). The first workshop was run in Torbay and South Devon NHS Foundation Trust and the second one at the Cochrane Colloquium (Edinburgh). The immersive part built on previous research on eliciting audience participation by providing a restrictive environment like a space mission rather than relying solely on pictorial realism. It included a virtual reality demonstration of a Soyuz spaceship leaving Earth followed by a live simulation of a spaceship accident. The latter was not intended to be realistic; it attempted to demonstrate some limiting aspects of a space mission. It included an individual in a fat suit, tinted glasses, and big gloves who was supported by suspension bands and could move around (the video is available via contacting with Mona Nasser). A second individual was present who was immobile and noncommunicative and dressed in a Biohazard decontamination suit. The room had limited lighting. There were some people in the room and some outside the room watching through a monitor (the mission control). There were clear problems with communications, and only certain people could talk. The simulation was of a post-accident scenario where an astronaut had to attempt to rescue an injured colleague whilst the responsible clinicians were based in mission control. Due to damage to the communication equipment, the remainder of the crew could only receive and pass information via mission control (simulated by the team in the sim suite control room) and direct their colleague. During the debriefing, the participants discussed the challenges of dealing with the limitations of the situations. They usually started to follow their standard emergency medical procedures. They did not consider that it might not apply to the unusual situation, for example, they first attempted to take the pulse through the artery—which was not possible when wearing the Biohazard "space" suit.

As the speculative scenario concerned an unexpected eye problem, we wanted to encourage the participants to think beyond the usual eye problems and expect unusual health/disease consequences. In any new context like Mars (or even certain situations on earth like outbreak of a new disease or monitoring adverse events of a new drug), you need to monitor for unexpected health/disease consequences. To achieve this, we provided the participants with the opportunity to use optical devices developed by Terry Pope (the hyperscope and the pseudoscope) which, through repositioning the eyes, simulate the possible perceptual changes which impact vision.[9] Please note it is not suggested that repositioning the eye is the consequence of long-term exposure to partial or microgravity; it was used as an example of an unexpected vision problem to demonstrate that new positive or negative health/disease consequences sometimes require a new and unfamiliar way for both the patients and clinicians to describe the problem and communicate the issues.

The immersive part was followed by an interactive discussion where participants worked through the eye problem scenario. Participants were asked to draw diagrams to demonstrate how they would structure the clinical research in this environment and how the different stakeholders and sections engage in different steps.

The second workshop did not include the immersive section and only included the speculative scenario of the eye problem and the interactive methodological diseases. The highly constrained scenario brought into sharp focus the importance of patient/consumer involvement in the design and conduct of research, the importance of informed consent and the challenges of maintaining equipoise.

The workshop participants included trialists, clinicians, patients, psychologists and individuals with art and humanity background.

3 | RESULTS

The issues and concepts identified as part of the workshops can be categorized as follows: (a) approaches to be inclusive in the management of the trial; (b) approaches to be inclusive in designing the research project (patient preference trials, N-of-1 trials, designing clinical

TABLE 3 Mars case scenario given to participants of the workshops

Item	Explanation
Case scenario	In a mission to Mars, there are 40-50 people who are staying on that planet for three years. You have increasing reports of individuals having differing eye problems, eg, blurriness, seeing spots, problems in seeing distance, etc. These eye problems are affecting the ability of individuals to perform their duties and affecting the mission in general. Moreover, it causes anxiety and stress as other members of the mission are worried that they might become affected. You need to come up with a solution to manage the situation and determine how to conduct clinical research that not only supports this mission but future ones. Note: The scenario is based on recent reports that some astronauts experience vision impairment that can last for a long time during and after space missions. The participants received quotes from astronauts that was available in publicly available documents, eg, a quote from astronaut Mike Baratt—"It's my right eye that has apparently been permanently remodeled." (Ref: NASA. Vision Impairment and Intracranial Pressure [VIIP]—05.02.18.) Available at: https://www.nasa.gov/mission_pages/station/research/experiments/1038.html.2018 and Silverman L. Doctor Launches Vision Quest To Help Astronauts' Eyeballs. Available at. https://www.npr.org/sections/health-shots/2017/03/04/518214299/doctor-launches-vision-quest-to-help-astronauts-eyeballs?t = 1536182114599. National Public Radio; 2017.
Discussion guide for workshop participants	How do individuals come up with potential interventions and prioritize those that could be used in clinical trials? Who do they involve in the decision-making process? How do they make decisions about what data to collect in order to evaluate the effectiveness of the interventions? Encourage people to think about clinical outcomes, biochemical and pathological outcomes along with performance outcomes. The latter is important for the mission, the former important for future missions. If people are familiar with clinical trial methodology, encourage them to think about ideas on how they would change the allocation, blinding or other aspects of the clinical trial. It will be helpful to encourage people to think and discuss ownership of clinical trials and the relationship of individuals in the mission with the leaders of the mission and how it can affect selection and allocation of individuals in the group as well as the overall social dynamic of the mission.

trials to be part of a future prospective meta-analysis, identifying biomedical, clinical, patient-related along be the performance-related outcome, data collection over time and monitoring need for adaptation and change); (c) balancing the research needs and the community needs (allocation of the participants based on both research and community need, for example, stratification not only based on characteristics but also by roles and job specification, using adaptive design to allocate individuals into groups and patient preferred trials); and (d) ethics and partnerships (ethics and consent issues and how they relate to partnerships and relationships).

3.1 | Approaches to be inclusive in the management of the trial

Astronauts have a lot of experience in conducting experiments as part of a daily routine in space missions, so we expect that being part of a clinical trial will be easier for them than standard patients. However, we do not know how human behavior changes or adapts on long-term missions and we expect that it will be more difficult—the isolation and separation from family and the different selection and training criteria, different cultures (both organizational cultures and country and ethnic culture) across space agencies. Therefore, it becomes more important to have a more collaborative approach in selecting the research questions that become the priorities for investigation in clinical trials on such missions. The workshop participants raised the issue that individuals view on the importance of outcomes changes as the health problem progresses over time. There is currently limited research on how these changes in priorities affect the view of the individuals on the effects of the intervention and how it would change the results if it is considered. We will explore this aspect in future workshops, and long-term Antarctica or Planetary Analog missions (currently these are mostly Mars and Lunar analog missions) are a potential environment to pilot and evaluate such strategies.

There were different approaches suggested to deal with these decisions around the selection and allocation of participants to the groups: (a) inclusive approach (some people use the term democratic approach) to rank the interventions—this could be either involving everyone or involving those who are affected in deciding which intervention has the highest potential and are most promising for addressing the health care problem; (b) approaching the manager of the mission or the leader that people listen to; and (c) build a committee of key individuals to make the decision.

The process not only depends on individual needs and values but also the expectations and prior agreements from the mission. The social and political impact of the clinical trial on the community was also discussed. These impacts might influence individuals' involvement in the research project and even the design of it. For example, certain expected adverse events from the treatment or consequences of the disease might lead people to prioritize specific interventions. The emergence of these effects can also influence the compliance of individuals throughout the trial.

3.2 | Approaches to be inclusive in designing the research project

One of the biggest challenges of aerospace medicine research is the low sample size as the number of astronauts is limited. This, unfortunately, is also often the case with simulation studies. Due to the technical requirements and costs, the number of individuals that can be recruited in space mission clinical trials is limited. Systematic reviews

with meta-analyses have been used to synthesize the data across clinical trials, and these can increase the power and generalizability of results. There is a possibility to address this issue using prospective meta-analysis, which requires the space agencies to plan the clinical trials, keeping in mind the future meta-analysis in which the clinical trial will be included. In this way, they could also plan those clinical trials over several space missions, especially as a health issue will probably come up repeatedly in future missions with new individuals.[10]

During the discussion around the speculative scenario, the question was raised whether this scenario challenges the notion that the standard RCT is the most appropriate methodology. The ethical challenges might favor alternatives such as N-of-1 or a stepped wedge. Regarding the aforementioned eye problem, in some cases, we might not be able to treat the problem and might need to find ways to ensure that the individuals manage symptoms to be able to perform their duties or live their lives. In these cases and these types of treatment, N-of-1 trials can be useful, so will be helpful if individuals have access to ways to incorporate these trials in their daily life.[11]

Given the small number of participants, difficulty to maintain equipoise and the ethics of the same population being involved, participants might favor an alternative. However, this issue was not raised in any of our workshops. In future workshops, we will explore whether the latter is a consequence of how the workshop was structured or the issue may not be considered relevant by the participants attending our workshop.

In both workshops, people raised the issue that not only would clinical and biomedical outcomes need to be collected, but also patient-related outcomes and performance-related ones (what people care about). There was also a discussion on unexpected outcomes, for example, unexpected side effects and the need to record and identify them. Some even suggested that we would collect data on each member's log (which does raise ethical and consent issues).

During the workshops, people raised concerns about a set of predefined and fixed outcomes at the beginning of the clinical trial. This is important to provide relevant comparison; however, people's priorities on what the most important outcomes are might change over time. Therefore, it has been suggested that the clinical trial team should have a continuous discussion with individuals in the group to see how the outcomes evolve.

3.3 | Balancing the research needs and the community needs

Clinical trials usually involve randomization in different treatment groups. We sometimes stratify individuals in the groups based on other confounders to explore their impact on the effectiveness of the intervention. During the workshops, the issue was raised that each person has a critical role in the mission. It's vital that if the performance of the individual is negatively affected by the trial (either that the intervention does not work or the intervention has side effects), that people with similar roles and job specification would not be in the same treatment group. Another reason for not having people with similar roles or similar living or working places to be in the same group is the possibility of contamination between groups. In these situations, one could implement stratified randomization to separate them by allocating them to groups. Moreover, the investigator could use weighted/unequal randomization which is still randomized but results in fewer participants allocated to the experimental group (or nonexperimental group whichever is deemed to have adverse consequences) (adaptive design).[11,12] There are alternative methods for designing the clinical trial which can be used, such as patient-preferred clinical trials, or different approaches to randomizing people to the groups, such as adaptive design clinical trials.

3.4 | Ethics and partnerships

The importance of partnerships and transparency was raised. It is vital to maintain the partnership and relations with the participants throughout the clinical trial. The workshop participants also raised the importance of implementing the results of the trial in the same population, and people need to see the benefit of doing a clinical trial to take ownership of it. In Edinburgh, we asked people how the discussion affected their views on conducting clinical trials on Earth, and this was one of the key aspects that they highlighted. The reality that the trial participants are also the trialists' community, colleagues and the patients made the participants of the workshop re-think how they would approach designing clinical trials. This is interesting considering the ethics of conducting clinical trials in developing countries, for example, outsourcing the commercial clinical trials to Latin America.[13]

Similar to the issue raised around Chris had field dilemma in the background;[6] the question was raised in the workshop, whether we require a different ethical paradigm for this type of research. Some questions raised were whether these interplanetary trial workshops impose decision-making from outside, or do they encourage methods for democratic decisions, where does it leave individual decision-making.

There was much discussion on challenges of randomizing people to one treatment group and one control/placebo group, especially if the intervention is codesigned with the participants and there is a level of anxiety over eyesight loss or adverse effects from the treatments. Some argued that people who sign up to such missions would be expected to have agreed to these types of experiments. However, social interaction, especially in difficult, complicated and stressful situations (losing eyesight can cause anxiety and stress), evolves in unpredictable ways, and it is important to consider how that affects people. Others suggested that if individuals are involved in designing the clinical trial and selection of intervention, they are more likely to accept the failure and adverse events. There were suggestions on the need to design appropriate placebos for such clinical trials.

4 | DISCUSSION

Although aspects of the experiment could have been predominately explored in a logical and narrative way, there are other social and

behavioral issues that require the participation of a wider audience to identify and unpick. The combination of simulation, optical devices and methodological discussions provided a helpful approach to achieve this.

Participants of the workshops found the interaction useful, not only to come up with new approaches to design clinical trials for interplanetary missions but also to reconceptualize clinical trials on Earth. For the participants, there was a realization that their evolving understanding of a new physical environment can lead to new ways to approach conduct clinical trials. In the first workshop, we explored the issue of challenging communication between the individuals in the spacecraft and mission control/support. However, we did not explore how mission control could help in the eye problem scenario in-depth. In some analog Mars missions, the mission support might have a better overview of the patterns of what happenings than clinicians involved. Although we primarily designed the workshop to understand how clinical trials might need to be changed for interplanetary missions, the workshop seems to be a very good training tool to engage a diverse group of individuals in the complexity of clinical trials and discussions on how to innovate the methods of clinical trials.

The current global pandemic outbreak of coronavirus raises questions, not only about how we manage the situation, but also about how we develop an infrastructure to collect data in a more systematic way to inform future decision making. Currently, many countries have chosen social distancing as an intervention to reduce the speed of the spread of the infection. However, good quality data will be key to understanding whether the long term benefits of the intervention outweigh its social and economic consequences. This project can be used to train individuals to find new processes and methods for unprecedented situations, such as disasters and pandemics.

5 | CONCLUSION

This methodology provides a useful approach to re-think the research methods to address a new challenge and problem and engage a wider range of individuals in those discussions. The main areas for discussion on innovation in this specific area (clinical trials in space missions) are: (a) approaches to be inclusive in the management of the trial (being inclusive in the management process); (b) approaches to be inclusive in designing the research project (patient preference trials, N-of-1 trials, designing clinical trials to be part of a future prospective meta-analysis, identifying biomedical, clinical, patient-related along be the performance-related outcome, data collection over time, and monitoring need for adaptation and change); (c) balancing the research needs and the community needs (allocation of the participants based on both research and community need, for example, stratification not only based on characteristics but also by roles and job specification, using adaptive design to allocate individuals into groups and patient preferred trials); and (d) ethics and partnerships (ethics and consent issues and how they relate to partnerships and relationships).

Speculative theorization using simulation and visualization grounded in evidence synthesis can be used for other methodological questions in aerospace medicine and wider health care research. For this specific topic, we intend to conduct additional workshops focusing on certain aspects of a clinical trial with a more diverse range of scenarios that include other types of health problems, for example, contagious ones or datasets that reflect the issues identified in this exercise.

ACKNOWLEDGMENTS

We would like to thank Eleanor Gonzaga, Klara Lucznic, Andrew Pugsley, Daniel Rose, Hans Lund, Klara Brunnhuber, Jennifer Yost for their input and contributions to developing the concept, material or commenting on the manuscript and we would like to thank Julian Wright, Daniel Rose and the rest of the VR team at Torbay Hospital for their amazing work and visualizations. We would also like to thank Terry Pope for providing the hyperscope and pseusoscope.

CONFLICT OF INTEREST

None.

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How to cite this article: Nasser M, Peres N, Knight J, et al. Designing clinical trials for future space missions as a pathway to changing how clinical trials are conducted on Earth. *J Evid Based Med*. 2020;1–8. https://doi.org/10.1111/jebm.12391